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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/421,545	10/20/1999	GREGORY R. MUNDY	432722002621	4287

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EXAMINER	
GITOMER, RALPH J	
ART UNIT	PAPER NUMBER
1627	

DATE MAILED: 08/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/421,545	Mundy et al.
Examiner	**Art Unit**
Ralph Gitomer	1627

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 28, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1 and 5-23* is/are pending in the application.

4a) Of the above, claim(s) *8-18* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 5-7, and 19-23* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

The IDS received 3/14/00 has not been considered because the references are not found in the file. The IDS received 9/10/01 has been considered. Priority is claimed to 7/10/1998. Please inform the examiner as to how the present application differs from the two parent applications, 09/361,775 and 09/113,947 to properly confirm the claimed priority date of 7/10/98. And please update the continuing information in the specification.

Applicant's election with traverse of Group I, claims 1-7, in Paper No. 8 is acknowledged. The traversal is on the ground(s) that the same search is required for Groups I and V. This is not found persuasive because claim 18 of Group V is directed to an independent invention with different limitations and functions than those of Group I.

The requirement is still deemed proper and is therefore made FINAL.

In paper #12 received 5/28/02 the bone formation species of claims 1, 5-7 have been elected in response to the requirement for election of species.

The inventor G. Rossini does not properly provide a first full name in the specification as originally filed or in the Declaration. Correction and a new Declaration with a full name is required. The full names of each inventor are required. Note the preferred spelling is ▒pentoxifylline▒.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5-7, 19-23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of copending Application No. 09/113,947, now allowed. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims are broader by including peptidyl

aldehydes among other compounds.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

What has been searched and considered here is:
A method of enhancing bone formation by administering a peptidyl aldehyde or pentoxifylline or epoxomicin. No references are cited teaching epoxomicin for bone formation.

Claims 1, 5-7, 19, 20, 22, 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of O'Keefe, Robin, Murray, and Woo.

O'Keefe (6,010,711) entitled ▒Methods, Articles and Compositions for the Pharmacologic Inhibition of Bone Resorption with Phosphodiesterase Inhibitors▒ with a 102(e) date of 1/1996 teaches in column 4 claim 1 pentoxifylline for inhibiting bone resorption.

Robin (J of Medicine) entitled ▒Study of Antiosteoporotic Agents in Tissue Culture▒ teaches in the abstract, pentoxifylline is an antiosteoporotic agent.

Murray (Exp Cell Res) entitled ▒The Ubiquitin Proteasome System and Cellular Proliferation and Regulation in Osteoblastic Cells▒ teaches in the abstract, parathyroid hormone feedbacks related to bone with lactacystin and MG-132 (Cbz-Leu-Leu-Leucinal), a peptidyl aldehyde, which are antiproliferative in osteoblastic cells. And that proteasome activities relates to osteoblastic function. See page 461 under Materials. On page 462 column 2 last full paragraph, studies show that proteolytic enzymes, such as the MCP (eukaryotic multicatalytic protease complex), are required for optimal osteoblastic cell

proliferation. Calpain effects on osteoblastic cells are discussed.

Woo (European J of Pharmacology) entitled ※Suppressive Effect of N-(benzyloxycarbonyl)-L-phenylalanyl-L-tyrosinal on Bone Resorption in vitro and in vivo※ teaches in the abstract, a peptidyl aldehyde inhibits bone resorption.

The claims differ from each of the above references in that the references do not all teach administering to an animal and do not teach additionally administering additional agents.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the claimed compounds to a human or other animal in view of each of the above references that teach administering to cell cultures or lower animals because such assays are generally accepted as indicating efficacy in humans. The present specification shows such assays. As for administering additional agents for the same function, this is common practice where combining known agents for the same function frequently has an additional beneficial effect over administering a single agent. No novelty is seen in administering compounds known for the claimed function irrespective of the underlying mechanism of action such as inhibiting proteasomal activity.

Claims 5 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 5 is directed to a number of disorders, many of which are notably difficult to treat effectively. Claim 22 is specifically directed to humans. The specification as originally filed provides no written description of treating any of the disorders in any vertebrate including humans.

Claims 1, 5-7, 19, 22, 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for PSI, does not reasonably provide enablement for ▒a peptidyl aldehyde▒. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In claim the terms "a peptidyl aldehyde" lack enablement as it would require one of ordinary skill in this art undue experimentation to determine which such aldehyde would work in the instant invention.

On page 35 Example 3 of the present specification shows data for PSI treating bone, on page 36 an unnumbered table indicates PS1 (not PSI) may be useful for bone formation.

The entire scope of the claims has not been enabled because:

1. Quantity of experimentation necessary would be undue because of the large proportion of inoperative compounds claimed.

2. Amount of direction or guidance presented is insufficient to predict which substances encompassed by the claims would work.

3. Presence of working examples are only for specific substances and extension to other compounds has not been specifically taught or suggested.

4. The nature of the invention is complex and unpredictable.

5. State of the prior art indicates that most related substances are not effective for the claimed functions.

6. Level of predictability of the art is very unpredictable.

7. Breadth of the claims encompasses an innumerable number of compounds.

8. The level of one of ordinary skill in this art is variable.

In re Wands, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)

The title of the invention is not aptly descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The Abstract of the Disclosure is objected to because it is not directed to the presently claimed invention. Correction is required. See M.P.E.P. § 608.01(b).

The following prior art pertinent to applicant's disclosure is made of record and not relied upon:

Mundy (6,410,512) is a related patent.

Meerovitch (J of Bio Chem) teaches proteasome function and parathyroid hormone effects.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ralph Gitomer whose telephone number is (703) 308-0732. The examiner can normally be reached on Tuesday-Friday from 8:00 am - 5:00 pm. The examiner can also be reached on alternate Mondays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (703) 308-4537. The fax phone number for this Art Unit is (703) 308-4556. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235. For 24 hour access to patent application information 7 days per week, or for filing applications electronically, please visit our website at www.uspto.gov and click on the button ※Patent Electronic Business Center※ for more information.

Ralph Gitomer
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RALPH GITOMER
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